

Growth curve for girls with Turner syndrome

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SUMMARY A growth chart for girls with Turner syndrome has been prepared using data from four published series of European patients, and evaluated using retrospective data on the heights of girls with Turner syndrome seen at this hospital. The results indicate that calculation of height standard deviation score from this chart allows a reasonable prediction of adult stature in any patient with Turner syndrome. In addition, the results indicate that while oestrogen treatment causes an initial acceleration of growth, it has no significant effect on adult height.

'How tall will she be when she grows up?' is an almost invariable question when the implications of Turner syndrome are explained to parents. To our knowledge, however, there are no growth standards that allow a fairly accurate prediction of adult height in any individual patient with the disorder. We have prepared a growth chart for girls with Turner syndrome, using data given in four previously published series of European patients. The value of this chart in predicting mature height has been evaluated using data on the heights of patients with Turner syndrome seen previously in the outpatient clinics of this hospital.

Method

The growth curve described in this paper has been derived from the mean heights and standard deviations (SD) at different ages in four published series of girls with Turner syndrome; namely 101 patients from Germany described by Pelz *et al.*,¹ 150 girls from Germany described by Ranke *et al.*,² 55 girls from Finland reported by Lenko *et al.*,³ and 60 girls from France reported by Rosenberg and Tell.⁴ In all these series the authors state that the patients had not received any hormone treatment.

Using the published means and SDs of each of the four studies, combined statistics were computed for each age group. Details of the method of calculation are given in the Appendix.

Height data were collected from the case notes of girls with Turner syndrome (45 X and various mosaics) who have attended this hospital. Patients treated with oestrogens were included but those given androgens were excluded. Age groups were defined so that, for example, age 10 years represented those measurements made between 9-51

years and 10-50 years. The mean height and SD were calculated for each age.

Results

Table 1 shows the mean heights and SDs at different ages calculated from the pooled data obtained from the four published series. The average SD for this composite curve is 4.7% of the mean height, which agrees with the average SD in each of the published series (3.7% to 5.1%, mean 4.5%).

Table 1 Height, mean (SD), at different ages calculated from four published series of girls with Turner syndrome and girls with this syndrome seen at this hospital

Age (yrs)	Data from published reports Height (cm)			Hospital for Sick Children Height (cm)		
	No	Mean	SD	No	Mean	SD
1	81	63.8	6.8 (3.0)*	11	64.9	3.7
2	52	77.5	3.5 (3.6)	12	74.9	4.3
3	64	84.2	4.7 (4.0)	15	83.1	4.4
4	58	91.1	5.5 (4.3)	9	88.3	4.7
5	66	96.5	5.0 (4.5)	9	92.7	5.4
6	79	103.1	6.4 (4.8)	12	97.8	4.0
7	77	106.0	5.0 (5.0)	14	102.3	5.1
8	83	111.4	6.6 (5.2)	11	105.2	4.6
9	97	115.0	5.7 (5.4)	26	112.5	4.9
10	93	119.5	6.4 (5.6)	44	116.7	4.6
11	84	122.8	6.2 (5.8)	55	119.8	4.6
12	105	126.5	5.9 (5.9)	49	123.0	6.6
13	85	130.7	5.8 (6.1)	70	128.1	6.0
14	85	132.6	5.9 (6.2)	79	131.3	6.3
15	84	135.8	5.7 (6.4)	84	134.2	5.9
16	84	138.6	5.4 (6.5)	79	138.3	5.8
17	52	140.6	6.0 (6.6)	42	139.1	5.2
18	26	143.4	6.3 (6.7)	26	139.2	3.8
19	24	143.2	6.1 (6.7)	28	142.8	3.7
20+	138	142.9	7.3 (6.7)	22	143.2	4.5

*Values in parentheses represent 'smoothed' SD taken as 4.7% of the mean value.

Figure 1 shows these data as mean (2 SD) plotted on a growth chart for normal girls⁵ taking the smoothed SD at each age as 4.7% of the mean height.

Table 1 also shows the mean (SD) height at different ages for 93 girls with Turner syndrome seen at this hospital. In general, the mean heights are lower than those for the pooled data, although by maturity there was no significant difference. Most of these girls had been treated with oestrogens from the age of 15 years, whereas the data from the published reports were for untreated patients only.

Twenty nine of the 93 girls seen at this hospital had been followed up until the ages of 19 to 24 years, and their growth seemed to be complete. Figure 2 shows the correlation between the height SD score (SDS) on the Turner growth chart when first seen in the outpatient clinics between the ages of 3 and 12 years (SDS_{initial}), and the SDS when last reviewed between the ages of 19 and 24 years (SDS_{final}). The correlation coefficient was 0.95 (P<0.001) and the regression equation:

$$SDS_{final} = 0.21 (0.07) + 1.13 (0.07) SDS_{initial}$$

with a residual SD of 0.30 SDS units and 95% confidence limits of the order of ±2.0 cm.

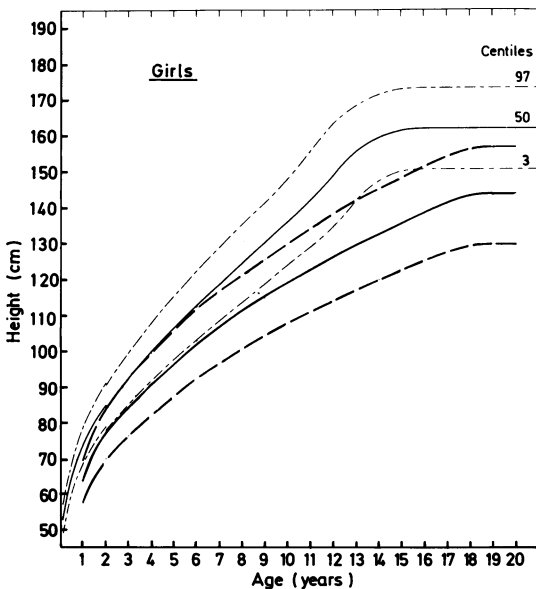


Fig. 1 Mean height (2 SD) at different ages calculated from published data on patients with Turner syndrome (heavy lines) plotted on a growth chart for normal girls (faint lines).

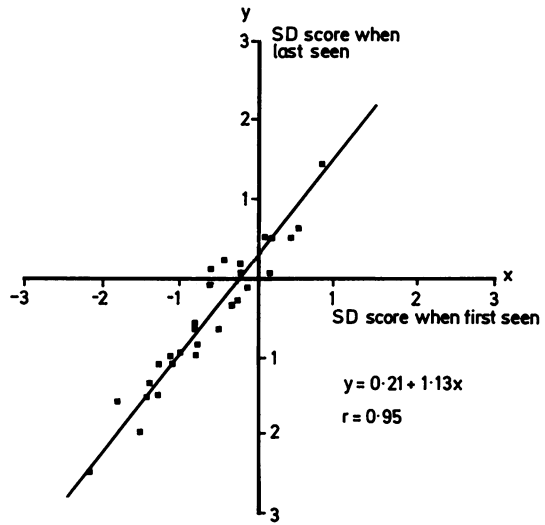


Fig. 2 Relation between height SDS on the Turner chart when first measured (age 3–12) and when last seen between the ages of 19 and 24 years in 29 girls with Turner syndrome.

In 12 girls, bone age was assessed at the time of the initial height measurement by the TW2-RUS method,⁶ and height predictions were made by methods applicable to normal girls.⁶ The mean error of mature height prediction was then +3.3 cm (that is overprediction) with a range between +19.7 and -3.3 cm. In contrast, using the growth chart described above, there was a trend to slight underprediction of height by an average of -0.6 cm. This underprediction was greatest (-3.8 and -1.9 cm) in the two girls with the greatest delay in bone age (5.4 and 4.4 'years' respectively). Although the bone age seemed relevant in these two examples, consideration of bone age delay did not generally improve the predictions in less extreme cases.

Table 2 shows the mean SDS on the Turner growth chart for the 29 girls at the time of presentation to outpatients, immediately before and one year after starting oestrogen treatment, and at the final visit to outpatients when aged 19 to 24 years. There was a significant improvement in the mean SDS one year after starting oestrogen (P<0.01, Student's paired *t* test) indicating that this treatment had accelerated growth. The mean SDS, however, when last seen in the outpatient clinic had almost returned to the value obtained when the patients were first seen, indicating that treatment had no significant effect on final height.

Eight girls, all with mosaic karyotypes, had spontaneous menarche between the ages of 13 and

Table 2 Mean standard deviation score calculated from the Turner chart in 29 girls: (a) when first seen, (b) immediately before, and (c) one year after starting oestrogen treatment, and (d) between the ages of 19 and 24 years when growth was complete

	Standard deviation score	
	Mean	SEM
(a) First visit	-0.60	0.10
(b) At start of oestrogen	-0.55	0.12
(c) After 1 year of oestrogen	-0.15*	0.09
(d) Last visit	-0.50	0.10

*Significant rise in mean SDS in the first year of oestrogen treatment; $P < 0.01$ —Student's *t* test.

17 years. Each had a growth spurt which started one to two years before menarche and over this period the mean SDS changed from -0.3 to a maximum of $+0.5$. Heights after the age of 19 years were available in only two of these girls. In one, the SDS_{final} remains significantly greater than the SDS_{initial} and in the other both SDSs were equal, suggesting that the growth spurt around the time of menarche had not improved final height in this girl (these two girls were not included in Fig. 2).

Discussion

The data used to construct the growth chart described above were obtained from four series of patients attending European centres—the series of Swiss patients described by Brook *et al*⁷ has not been included as mean heights without SDs are given in this paper, precluding the incorporation of the data into the composite growth chart.

As there are significant differences in height in different populations, even within northern Europe, the above growth curve will not necessarily represent the actual range of height of girls with Turner syndrome in any given population. For example, the mean heights of the girls seen in London at different ages were generally lower than the combined mean values from the other European centres. The data obtained, however, from the UK indicated quite clearly that in most patients with Turner syndrome there is a close relation between height during the first decade and adult height. It follows that the growth curve described above could have been used to predict final height with a fair degree of accuracy in these patients, simply by calculating the height SDS at presentation and using this SDS to calculate mature height. As would be expected the accuracy of the prediction could have been improved by using the regression equation given above. In girls with extreme delay in skeletal maturation the prediction

would probably have been unduly pessimistic; the reverse may be true in girls with advanced skeletal age, but no such patients were present in our small sample.

The relatively poor performance of the multiple regression prediction equations⁶ is not surprising as they were developed from groups of *normal* children who all underwent an adolescent growth spurt, and assume that such a spurt will occur in the test population. Further, it is well recognised that the maturation of the wrist and hand bones in Turner syndrome are discordant and it might be expected that assigned bone age scores would not reflect maturation correctly.

Several authors have reported that there is no significant difference in adult height between patients with 45 X karyotypes and patients with mosaic forms of Turner syndrome, although the mosaic patients were taller in the series reported by Snider.⁸ In patients seen at this hospital, there was no significant difference in the mean SDS for the 45 X patients and the SDS for those with mosaic karyotypes. Although the growth curve described above was derived from mixed data for patients with 45 X karyotypes and different types of mosaicism, it seemed to be useful in predicting adult height in both these groups of patients.

The growth chart may also be of value in evaluating treatment aimed at increasing final stature in patients with Turner syndrome, for example, the use of anabolic steroids. Our own data do not shed any light on this point as none of the patients who had been followed until growth was complete received such treatment. The results, however, do give further information on the effects of oestrogen treatment on final height in Turner syndrome. This treatment results in a growth spurt, as shown by the change in SDS during the first year of treatment. By the age of 19 years or more, however, most patients had returned to the height centile from which they started, and there was no significant difference between the mean SDS when first seen and that obtained when growth was complete. These observations strongly suggest that treatment with oestrogen at the age of normal puberty had had very little influence on final height.

Appendix

In what follows \bar{x} , s , and n are used to symbolise the mean height, the standard deviation, and the number of observations respectively. Subscripts *i* and *a* are used to indicate the study (*i* = 1 to 4) and the age group (*a* = 1 to 20). Thus \bar{x}_a = mean height for age *a* combining the data from all four series, whereas \bar{x}_{ai} would represent any of the four means from the separate studies, but all at age *a*.

For each age the mean height was calculated as:

$$\bar{x}_a = \frac{\sum_{i=1}^{i=4} n_{ai} \bar{x}_{ai}}{\sum_{i=1}^{i=4} n_{ai}} \quad (1)$$

Generally the standard deviation, *s*, can be calculated from the equation:

$$s = \sqrt{\{\sum x^2 - (\sum x)^2/n\}/(n - 1)} \quad (2)$$

which is identical to:

$$s = \sqrt{\{\sum x^2 - n\bar{x}^2\}/(n - 1)} \quad (3)$$

which by rearrangement gives:

$$\sum x^2 = (n - 1)s^2 + n\bar{x}^2 \quad (4)$$

and thus the four sets of $\sum x_{ai}^2$ could be calculated at each age from the known values of s_{ai} , \bar{x}_{ai} , and n_{ai} , for each age in each series. The combined values of $\sum x_a^2$ were thus calculated for each age by simple addition of the $\sum x_{ai}^2$. For the pooled data n_a was known as was \bar{x}_a from equation (1) and therefore s_a for the four studies combined could be calculated from equation (3), for each age group. The values of n_a , \bar{x}_{ai} and s_a are given in Table 1.

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Received 11 April 1985